

Drugs causing Methemoglobinemia in Children

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ABSTRACT

Methemoglobinemia is the rare disorder of the blood in which there is an increase in the proportion of haemoglobin present in the oxidized form (Methaemoglobin). Methaemoglobin is oxidised form of the iron moiety (Fe^{3+}) within the haemoglobin (HB)molecule.[2]

Drugs rarely causes the Methemoglobinemia in adults in comparative to Children. Common Drugs causing methemoglobinemia in children are Antibiotics (Dapsone, sulfamethoxazole), local anaesthetics (procaine, lignocaine) antimalarial drugs (quinine derivatives), antineoplastic drugs.

Most common drug causing methemoglobinemia is Dapsone

Children with reducing reductase deficiency or abnormal haemoglobin may exhibit severe effects as well as overdose.

Keywords: Breathing difficulty, Dapsone, Cyanosis, Methemoglobinemia, Acquired Methemoglobinemia.

INTRODUCTION:

Methemoglobinemia is a rare disorder of the blood in which there is an increase in the proportion of haemoglobin present in the oxidized form (methaemoglobin)[1].

Methaemoglobin is oxidised form of the iron moiety (Fe^{3+}) within the haemoglobin (HB)molecule.[2]

Drugs rarely causes the Methemoglobinemia in adults in comparative to Children. Common Drugs causing methemoglobinemia in children are Antibiotics (Dapsone, sulfamethoxazole), local anaesthetics (procaine, lignocaine) antimalarial drugs (quinine derivatives), antineoplastic drugs.

Children with reducing reductase deficiency or abnormal haemoglobin may exhibit severe effects as well as overdose.[3]

Methemoglobinemia caused by overdosing of some of the drugs. Administration or expose to the low doses of drugs for prolonged period may leads effect on Haemoglobin. Some of the common drugs causing Methemoglobinemia in children are Antibiotics (Dapsone,

sulfamethoxazole), local anaesthetics (procaine, lignocaine) antimalarial drugs (quinine derivatives), antineoplastic drugs.

- Antibiotics: Dapsone is the most common drug causing Methemoglobinemia in children.

Dapsone (DDS-diaminodiphenylsulphone), is a sulfone antibiotic used in the treatment of leprosy and for dermatological disorders [4]. Although dapsone poisoning was more frequent in the past [5], it is becoming less common in children. There are only few case reports on dapsone poisoning in children in recent years [6-10]. The most frequent complication of dapsone poisoning in children is haemolytic anaemia and methemoglobinemia [11]. The level of methemoglobinemia determines the poisoning symptoms and severity. At the lowest level of methemoglobinemia (<30%), child could be asymptomatic; as the level increases it may present with headache, lethargy, tachycardia, dizziness may occur (6). Further increase in methemoglobinemia may result in progressively dyspnoea, acidosis, seizures, cardiac dysrhythmias, heart failure, coma and even death when methemoglobinemia is high (>70%) [6]. The treatment of dapsone intoxication is oral administration of activated charcoal and intravenous administration of methylene blue for symptomatic methemoglobinemia. Gastric decontamination and early administration of serial oral activated charcoal is effective in reducing further absorption. Although, haemolysis can be mild, transfusions may be required for patients with a glucose-6-phosphate dehydrogenase deficiency (9) or in situations where methemoglobinemia is not controlled. Below a case of Dapsone poisoning in 8 year old child is presented.

2. CASE REPORT:

8-Year-old child presented with irritability, restlessness, breathing difficulty 1 day prior to accidental ingestion of 10 dapsone tablets. The drugs had been taken by father for the treatment of leprosy. Child had bluish discolouration of lips and tongue. On examination revealed central cyanosis, pulse rate of 116beats/ min regular, good volume, respiratory rate of 48 breaths/min with intercostal and subcostal recession, BP 100/60 mm Hg. Systemic examination was showed to have PEM, Weight was 16 kg and Height was 112 cm, Blood was drawn for investigation was chocolate brown in colour, it did not change colour when oxygen was bubbled through it. Haemoglobin-8 mg/dl, blood urea-42 mg/dl, serum electrolytes Na⁺-137, K⁺-4.2, chest x ray and ECG were normal was normal.

Methaemoglobin level was 20% at admission. Child was started supportive treatment and gastric lavage. The child was admitted and given activated charcoal orally with immediate intravenous administration of methylene blue at 2 mg/kg of 1% solution. Half of the initial dose was repeated after 5hrs, child did not show much improvement methylene blue level decreased to 15%. Correction of metabolic acidosis and administration of Ascorbic acid 500 mg intravenously was given, intravenous ascorbic acid 100 mg twice daily was continued. In spite of the treatment Methaemoglobin level was not reduced. Exchange transfusion was done after Methaemoglobin is drop to 10% and child improved drastically thereafter. On follow up no sequelae were found

3 DISCUSSION

Accidental dapsone is a pediatric emergency in young preschool children [5]. Dapsone a sulfone is well absorbed on oral ingestion with peak levels after two or three hours. The drug can be detected in tissues up to three weeks after ingestion. It causes methemoglobinemia resulting in cyanosis. The clinical symptoms vary and depend upon on methemoglobin concentration in blood [12]. Methemoglobin is incapable of binding oxygen and also increases the affinity for unaltered hemoglobin for oxygen, shifting the oxygen dissociation curve to left thus further improving oxygen delivery resulting in dyspnoea. The CNS

manifestations are irritability, hypotonia, truncal ataxia, choreiform movements and dysarthric speech [7-10].

Direct effect of drug on CNS and cerebral anoxia is due to methemoglobinemia. In acute dapsone toxicity initial attempts should be given to gut decontamination. And improvement of oxygen delivery, main emphasis on administration of methylene blue and ascorbic acid. Methylene blue given intra venous is rapidly reduced in to leukomethylene blue then becomes available to reduce methemoglobin to hemoglobin. It is the mainstay of the treatment of methemoglobinemia. In less severe cases ascorbic acid 200-500mg can be given iv (6). Exchange transfusion can be tried in cases not responding to methylene blue [12].

It is suggested that cases previously perfectly normal and presenting with unexplained central cyanosis with history of ingestion of dapsone be considered as having Methemoglobinemia. Dapsone a commonly used drug in the treatment of leprosy should be kept out of reach of children to prevent significant morbidity and mortality. Exchange transfusion had been reported to be very effective in the management of Methemoglobinemia (12).

- Local Anesthesia causing Methemoglobinemia

Methemoglobinemia can occur following use of prilocaine in adults. In adults, the toxic dose is ~ 600 mg IV. Prilocaine is metabolized by the liver to O-toluidine, which oxidizes hemoglobin (Fe²⁺) to methemoglobin (Fe³⁺). This can also occur with EMLA cream, especially in neonates 3 months or younger (although still safe in the vast majority of neonates). Treatment is with methylene blue [13-14]

- Nitrates causing Methemoglobinemia

Acquired methemoglobinemia is known to occur due to reduction of haemoglobin to methaemoglobin and is commoner than the congenital variety. It may occur due to drugs such as benzocaine, lidocaine, flutamide, dapsone, nitrites, phenazopyridine, amiodarone, amyl nitrite, primaquine, chloroquine, quinones, sulphonamides acetaminophen, hydrogen peroxide, disulfiram, ibuprofen, and metoclopramide.

High levels of nitrate and nitrites in some vegetables (eg: carrot, beetroot, radish juices) have been reported, depending upon factors such as fertilizer use, method of storage, bacterial contamination, and method of preparing (eg: removal of stems, peeling, blanching). Although the adverse health effects of dietary nitrate and nitrite are uncertain, consumption of home-made and small-scale industrially produced raw vegetable juices (eg: use of beetroot juice to improve athletic performance) may lead to unacceptably high levels of nitrite intake, increased nitric oxide production and possibly increased risk of methemoglobinemia.[15-16]

- Antimalarial drug causing Methemoglobinemia

Most common antimalarial drug causing methemoglobinemia is Primaquine. Primaquine is particular known to cause Methemoglobinemia in toddler age group due to overdosage during antimalarial therapy. paediatric patients represent the vast majority of known primaquine overdoses. Their diagnosis and treatment require good working knowledge of antimalarial toxicities and management options of children.[17]

CONCLUSION:

In the Paediatric age group, children are very much sensitive to the drugs and their effects on the body. The accurate diagnosis and treatment require the good knowledge about the drugs prescription is very much important for the children. Continuous administration of the drugs and overdosage of the drugs may leads to the clinical condition such as Methemoglobinemia. Methemoglobinemia is the rare disorder of the blood in which there is an increase in the proportion of haemoglobin present in the oxidized form (Methaemoglobin). Methaemoglobin is oxidised form of the iron moiety (Fe^{3+}) within the haemoglobin (HB)molecule.[2] Drugs rarely causes the Methemoglobinemia in adults in comparative to Children. Common Drugs causing methemoglobinemia in children are Antibiotics (Dapsone, sulfamethoxazole), local anaesthetics (procaine, lignocaine) antimalarial drugs (quinine derivatives), antineoplastic drugs.

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